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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/749,703	12/31/2003	Rodney Alan Jue	219002031111	9327
25225	7590	08/29/2006	EXAMINER	
MORRISON & FOERSTER LLP 12531 HIGH BLUFF DRIVE SUITE 100 SAN DIEGO, CA 92130-2040			ALLEN, MARIANNE P	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 08/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/749,703

Applicant(s)

JUE ET AL.

Examiner

Marianne P. Allen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-42 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION***Priority and Oath/Declaration***

Claims 1-42 are the originally filed claims in the instant application. It is noted that this application is stated to be a divisional application of 09/575,199. However, parent application 09/575,199 was filed with claims 1-74. Present claims 1-42 do not correspond to any originally filed claim in 09/575,199 although there is some similarity to claims 35-64 of this parent application. For example, there does not appear to be any originally filed claim in 09/575,199 that specifies removal of the N-terminal sequence is performed by diaminopeptidase enzymatic digestion (see instant claim 8). For example, there does not appear to be any originally filed claim in 09/575,199 that specifies that 95% of VEGF dimmers are devoid of an N-terminal methionine residue when the amino acid sequence is extended by a Met-(AA)_n sequence at the N-terminus (see instant claim 9). Note that originally filed claim 35 in 09/575,199 was directed to a process for providing a composition of matter comprising VEGF polypeptides comprising **at least two dimers**, and that the instant claims are providing a single dimer.

The subject matter of instant claim 11, 23, 28, and 42 does not appear to have been previously claimed. The subject matter of claims 24-42 with the glycosylation mutation and bonding to an extraneous Cys does not appear to have been previously claimed.

As such, this application is considered to be a continuation-in-part and not a divisional application. This application presents claims for subject matter not originally claimed or embraced in the statement of the invention. A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly

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identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Applicant is requested to update the continuing information in the first line of the specification and correctly identify the instant application as a continuation-in-part.

Applicant is requested to point to antecedent basis in the specification for the limitations for claims 1-42 because they are not apparent. Applicant is reminded that the specification is required to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o).

Applicant is advised that this application **as filed** remains a continuation-in-part of the parent application even if the instant claims are amended to correspond to those of the parent application.

Applicant is denied priority to parent application 09/575,199 as basis is not seen for claims 1-42 in the parent application. Applicant is denied priority to provisional application 60/135,312 and 60/177,407 as basis is not seen for claims 1-42 in these applications. It is further noted that 60/135,312 mutates the cysteine at position 116 to serine rather than leaving it intact as in the instant methods and that 60/177,407 does not disclose the extension at the N-terminus. The effective filing date for claims 1-42 is considered to be 12/31/2003.

Claim Rejections - 35 USC § 112

Claims 1-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

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was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable producing VEGF dimers with a Cys at 116 of SEQ ID NO: 1 or an Asn-to-Glu amino acid substitution at position 75 of SEQ ID NO: 1. SEQ ID NO: 1 is a nucleic acid and SEQ ID NO: 2 which is the corresponding amino acid sequence does not have Cys at 116 nor Asn at 75. As such, the specification does not give clear guidance as to what VEGF dimers within the scope of the claims should be produced and how to do this.

Claims 1-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-42 refer to the amino acids of SEQ ID NO: 1. SEQ ID NO: 1 is a nucleotide sequence and not an amino acid sequence. It appears that SEQ ID NO: 2 may have been intended as this appears to be the amino acid sequence corresponding to SEQ ID NO: 1. However, this is would also be confusing as SEQ ID NO: 2 does not have Cys at amino acid position 116. It has His. Claims 24-42 refer to

Claims 1 and 24 recite “at or corresponding to position 116.” Claim 12 recites “a position corresponding to position 116.” This is confusing. Particularly in view of the above discussion, it is unclear what this position corresponds to. The claims embrace larger sequences, including N-terminus extensions, and those that have at least about 90% sequence identity with amino acids 11-116 of SEQ ID NO: 1. As such, any cysteine

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present could be considered the “corresponding” one in the absence of other required structural or functional characteristics. Claim 24 is also unclear for the same reason for the recitation of “Asn-to-Glu amino acid substitution at or corresponding to position 75 of SEQ ID NO: 1.”

Claim 9 is confusing in requiring that at least 95% of VEGF dimers are devoid of an N-terminal methionine. Claim 1 (upon which it depends) requires addition of an N-terminal methionine and there are no steps in claim 1 or 9 to remove this residue. Claim 27 is similarly confusing in its dependence on claim 24.

Claim 11 is confusing in reciting “produce desired mixture of dimers.” There is no antecedent basis for producing multiple varieties of dimers or in particular mixtures. Claim 42 is similarly confusing.

Claim 12 is confusing in reciting in the preamble that “each monomer is disulfide bonded to an additional extraneous Cys” but having no step in the body of the claim that would provide that result. In addition, the claim does not have any explicit step by which the VEGF monomers form dimers.

Claim 28 is confusing in failing to provide a clear step by which “each monomer is disulfide bonded to an additional extraneous Cys.”

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant

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for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 10-16, and 20-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Alitalo et al. (U.S. Patent No. 6,965,010 B2).

The effective filing date for the instant application is 12/31/2003 for the reasons set forth above. As such, Alitalo et al. is valid prior art under 102(e).

For purposes of applying art, it is assumed that SEQ ID NO: 2 was intended (see 112, 2nd rejections above).

Alitalo et al. discloses producing VEGF dimers in bacterial cells using an N-terminal Met-Lys extension. All 8 cysteines involved in dimerization are retained in the hybrid constructs. The dimers are produced in the presence of glutathione. See abstract; claims, particularly claims 1-6; columns 13-18, particularly column 17, lines 40-50; column 27, lines 1-16; and Examples 1, 14, and 16.

Amino acids 1-140 of SEQ ID NO: 2 of the instant application corresponds to amino acids 1-140 of SEQ ID NO: 2 of Alitalo et al. Several embodiments include amino acids 1-135 of SEQ ID NO: 2. This would meet the sequence limitations of the claims as several cysteines are present and are deemed to meet the limitation of corresponding to position 116. Absent evidence to the contrary, producing the dimers in the presence of glutathione would inherently result in a cysteine being disulfide bonded to an extraneous cysteine.

Conclusion

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Friday, 5:30 am - 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Marianne P. Allen
Primary Examiner
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8/23/06

mpa